

REMARKS

Pursuant to the entry of the instant amendment, Claims 1-5 and 10, 11, 13, and 14 are pending. Claims 4, 5, 10 and 11 are allowed; and Claims 6-9 and 12 are cancelled.

I. Claim Rejections under 35 U.S.C. §102

The Examiner has rejected Claims 1, 3, and 13 under 35 U.S.C. §102(a) as being anticipated by Murakami (J. Bacteriol., April 2002, 184, 7, 1998-2004). In particular, the Examiner stated that "Murakami *et al.* disclose a method of modulating Sec-depdependent protein secretion comprising providing a *Bacillus* cell comprising *spoIIIJ* and *yqjG* genes linked to an endogenous high expression promoter and modulating their expression by varying the level of induction of said promoter".

Applicants respectfully traverse the rejection for the following reasons. Applicants' present application claims priority to US provisional application 60/348,080 filed January 9, 2002, hereinafter referred to as '080. The '080 application provides support Claims 1, 3 and 13 as follows. The '080 application "provides for the efficient secretion of proteins of interest from a gram-positive host cell. Preferably, the host cell is a *Bacillus* cell " (see lines 26-27 at page 7). The '080 application also provides for "a DNA construct for the inducible expression of the *spoIIIJ* gene. The *spoIIIJ* gene is operably linked to a promoter sequence. The promoter sequence may be either inducible or constitutive." (see page 7, lines 28-30). A DNA construct comprising the *spoIIIJ* gene operably linked to a constitutive promoter (the PSAC promoter) is shown in Figure 2 and described at least in the description of Figure 2 at page 8, line 23 to page 9, line 10). Modulation of secretion of a protein of interest e.g. AmyQ resulting from the inducible transcription of the *spoIIIJ* gene is shown at least in Figure 4, which discloses the results of experiments described in Example 6 (see page 25, line 5 to page 27, line 3). Figure 4A, for example, shows that the levels of AmyQ secreted into the medium of a culture of *B. subtilis* double mutant lacking *yqjG* and expressing none or "limiting amounts of SpoIIIJ (no or 50nM IPTG) is about 5-fold reduced when compared to those in the media of the fully induced double mutant (500nM IPTG), or the parental strain

168." (see Page 25, line 28 to page 26, line 3). Further, Applicants noted that while "the SpoIIJ-depleted double mutant cells also contained significantly decreased levels of mature AmyQ", and that "the SpoIIJ-depleted double mutant cellular levels of pre-AmyQ were not significantly affected by SpoIIJ depletion in the absence of YqjG (Fig. 4A, upper panel)", which indicate that the sec-dependent processing of the pre-AmyQ protein to the mature AmyQ protein and its secretion is compromised in the absence of the *yqjG* gene and depletion of the SpoIIJ protein. Applicants also disclose that "cells with limiting amounts of SpoIIJ /YqjG have a general defect in protein secretion" (see page 26, lines 3-11).

Therefore, the '080 application provides support for Claims 1, 3 and 13.

The article by Murakami et al. was published in April 2002, after the filing date of the '080 application. Therefore, Murakami et al. cannot anticipate Claims 1, 3 and 13 under 35 U.S.C. §102(a).

Based on the foregoing, Applicants respectfully request that the rejection of Claims 1, 3, and 13 under 35 U.S.C. §102(a) be withdrawn.

II. Claim Rejections under 35 U.S.C. §103

The Examiner has rejected Claims 1-3, and 14 under U.S.C. §103(a) as being unpatentable over Murakami *et al.* in view of Vagner *et al.* (Microbiology, 144, 3097-3104, 1998). In particular, the Examiner cites Murakami et al. "essentially for the reasons set forth above" (see office action page 3), discloses that Vagner *et al.* disclose the Pspac promoter for use in *Bacillus subtilis* gene expression, and states that "it would have been obvious to have used the well known and studied promoter which is Pspac".

Applicants respectfully traverse the rejection for the following reasons.

As discussed above, Murakami *et al.* does not anticipate Claims 1, 3 and 13. Vagner *et al.* does not teach a method of modulating Sec-dependent protein secretion as recited in Claims 1, 3 and 13. Therefore, Vagner *et al.* does not teach nor does it render obvious all the elements of Claims 1, 3 and 13 within the meaning of 35 U.S.C. §103(a).

In light of the foregoing Applicants respectfully request that the rejection of Claims 1, 3, and 13 under 35 U.S.C. §103(a) be withdrawn.

III. Claim rejections under 35 U.S.C. § 112

The Examiner rejected Claims 6, 12, and 13 under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In order to expedite prosecution and yet without acquiescing to the Examiner's arguments, Applicants have cancelled Claims 6 and 12, without prejudice.

In respect of Claim 13, and according to the Examiner's interpretation of the claim, Applicants have amended the claim to recite "inducible" when in reference to the promoter, and have deleted the term "high expression".

Applicants respectfully request that the rejection of Claims 6, 12 and 13 under 35 U.S.C. §112, second paragraph, be withdrawn.

CONCLUSION

Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7636.

This paper is accompanied by a request for Extension of Time under 37 C.F.R. 1.136(a) of THREE months extending the time for response to September 21, 2008. This response is filed prior to the extended deadline and is therefore timely filed. The Commissioner is authorized to charge any fees that may be required in connection with this submission and to credit any overpayments to Deposit Account No. 07-1048 (Attorney Docket No. GC715-2-US).

Respectfully submitted,

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